STRUCTURE ACTIVITY TEAM REPORT ver. 04/98 [redacted]

Case #: P-08-0508-509	DCN:
SAT Date: 7/11/2008	SAT Chair: L. Keifer

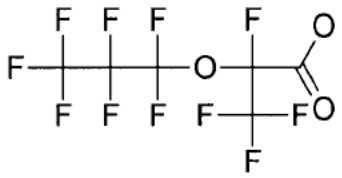
Submitter: DuPont

Chemical Name:

Propanoic acid, 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy)-

CAS RN:	Trade Name:
13252-13-6	None

Structure



[redacted]

Molecular Formula:	$C_6HF_{11}O_3$		
Molecular Wt. 330	WT%<500:	WT%<1000:	
MP:	BP: [redacted]	Eq. Wt:	
H2O Sol (g/L): 0.043	V.P. [redacted]		
Max. Prod. Volume (kg/yr): [redacted]	Physical State: [redacted]		

USE:

Chemical intermediate for [redacted], P-08-509 ([redacted]) [redacted] for polymerization aid ([redacted])
STN file CA 53 references found

Related Case Numbers	Case Role	Related Case Numbers	Case Role
[redacted]		[redacted]	

Focus Date: 7-24-08 Results: SR-Health, PBT

STRUCTURE ACTIVITY TEAM REPORT ver. 04/98	[redacted]
Case #: P-08-0509	**DCN:**
SAT Date: 7/11/2008	**SAT Chair:** L. Keifer

Submitter: DuPont

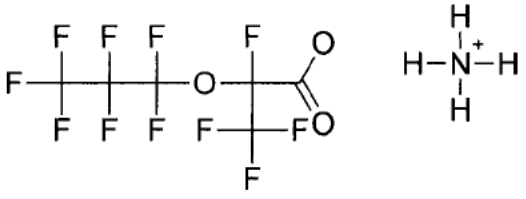
Chemical Name:

Propanoic acid, 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy)-, ammonium salt (1:1)

CAS RN: 62037-80-3

Trade Name: None

Structure



[redacted]

Molecular Formula:	$C_6H_4F_{11}NO_3$		
Molecular Wt. 347	**WT%<500:**	**WT%<1000:**	
MP:	**BP:**	**Eq. Wt:**	
H2O Sol (g/L): Dispersible	**V.P.** [redacted]		
Max. Prod. Volume (kg/yr): [redacted]	**Physical State:** [redacted]		

USE:

Polymerization aid - internal (95.7%) and external (4.3%) use
STN file CA: 12 references found for use as a surfactant.

Related Case Numbers	Case Role	Related Case Numbers	Case Role
		[redacted]	

Focus Date: 7-24-08 Results: SR-Health, PBT

STRUCTURE ACTIVITY TEAM REPORT [redacted] 07/11/08

CASE NUMBER: **P08-0508/0509**

RELATED CASES: [redacted]

CONCLUSIONS/DISCUSSIONS

TYPE OF CONCERN:	HEALTH	ECOTOX
LEVEL OF CONCERN:	2-3	2

KEYWORDS: MUTA IRR/CORR-E,MM,L,S
LIVER BLOOD KIDNEY
HEART LUNG ONCO
AQUATOX

SUMMARY OF ASSESSMENT

FATE: **0508**: [redacted] with MP < 25 °C (E)
log Kow = 3.66 (E);
S = 205 mg/L at 25 °C (E)
VP = [redacted] (M)
BP = 173 °C (NOMO5) based on [redacted]
H = 2.05E-4 (E)
log Koc = 2.08 (E)
log Fish BCF = 0.50 (E)
POTW removal (%) = 0
Time for complete ultimate aerobic biodeg > mo
Sorption to soils/sediments = low
Volatilization half-life from a standard river = 7 hrs
Volatilization half-life from a standard lake = 10 da
Atmospheric Oxidation Half-life = 250 hr via OH radical
PBT Potential: P3B2T3
*CEB FATE: Migration to ground water = rapid

0509: Estimations for the covalent ion pair MW 347 $C_6H_4F_{11}NO_3$
Solid with MP = 127 °C (E)
log Kow = 0.78 (E);
S = Disp./1.4 g/L at 25 °C (ICB/E)
VP < 1.0E-6 torr at 25 °C (E)
BP > 400 °C (E)
H < 1.00E-8 (E)
log Koc = 2.91 (E)
log Fish BCF = 0.50 (E)
POTW removal (%) = 0; OECD111(Hydrolysis): t1/2(pH4,7,9 at 50C): >1yr (0%/5d); OECD301B(Mod Sturm CO2 ev): 0%/28d.
Time for complete ultimate aerobic biodeg > mo
Sorption to soils/sediments = low
PBT Potential: P3B2T3
*CEB FATE: Migration to ground water = rapid

HEALTH: **0508**: Absorbed all routes (analog). **0509**: Expect poor absorption from the skin, good absorption from the lung and GI

tract (analog). Concern for mutagenicity; liver, blood, kidney, and heart toxicity; corrosion to all tissues (508), dermal sensitization (508) based on submitted test data; and lung toxicity (509) based on surfactant properties. Concern for oncogenicity based on C_6 and C_8 perfluoroacids.

*CEB HEALTH: Moderate high concern (Dermal, inhalation, drinking water, fish ingestion)

Test data: **0508**: (-) Salmonella with and without activation; (-) E. coli with and without activation; (+) for chromosome aberrations in CHO cells with and without activation for polyploidy; (-) for chromosome aberrations in CHO cells with and without activation for structural changes; rat oral LD_{50} = 550 mg/kg (F); corrosive to skin using the *in vitro* Corrositex assay; rat clearance time following oral administration: 28 (M) & 8 (F) h at 10 mg/kg, 22 (M) & 4 (F) h at 30 mg/kg; rats dosed orally at 30 mg/kg for 7 days had increased liver weight and liver toxicity; rat 14-day oral LOEL = 30 mg/kg, liver, blood, and kidney toxicity; (+) for skin sensitization in mice using the local lymph node assay with EC_3 = 37%; no metabolism by rat hepatocytes *in vitro* in 2 h

0509: (-) Salmonella with and without activation; (-) E. coli with and without activation; (+) for chromosome aberrations in CHO cells with and without activation for crude material, (+) with activation for a purified material for structural changes; equivocal (+) for chromosome aberrations in CHO cells with and without activation for polyploidy; (-) in an oral mouse micronucleus assay; (-) in a rat hepatocyte UDS assay *in vitro*; (-) in a mouse *in vivo* chromosome aberrations assay; (-) in an *in vivo* rat UDS assay; no skin irritation in rabbits; mouse oral LD_{50} = 1030 mg/kg (F); rat oral LD_{50} = 1750 mg/kg (M), 3129 mg/kg (F); rat oral ALD = 7500 mg/kg, liver toxicity; rabbit dermal LD_{50} >5000 mg/kg, necrosis of skin; rat dermal LD_{50} >5000 mg/kg, necrosis of skin; rat clearance time following oral administration: 12 (M) & 4 (F) h at 10 mg/kg, 22 (M) & 8 (F) h at 30 mg/kg; mice dosed orally for 7 days with 30 mg/kg had increased liver weight and liver toxicity; rat 14-day oral LOEL = 30 mg/kg with blood, liver, kidney, and heart toxicity; no skin sensitization in mice using the local lymph node assay

[redacted]

P08-0088: negative in Salmonella and E coli
uncertain positive for chromosome aberrations in CHL cells, positive results seen at the threshold of or beyond the point of cytotoxicity
28-day oral study in rats - NOEL = 5 mg/kg; hematological findings and changes in blood chemistry at 100 mg/kg; effects on the liver , kidneys, and forestomach at 100 mg/kg; increased kidney weights at 25 and 100 mg/kg
pharmacokinetic study in rats, iv administration - systemic exposure was 7 times higher in males than females; serum half-life = 9.4 hours in females and 5.4 hours in males
pharmacokinetic study in monkeys, iv administration - pharmacokinetic parameters in serum were similar between genders; males appeared to have a higher exposure and longer half-life than females
acute oral study in rats - LD50 = 500 mg/kg

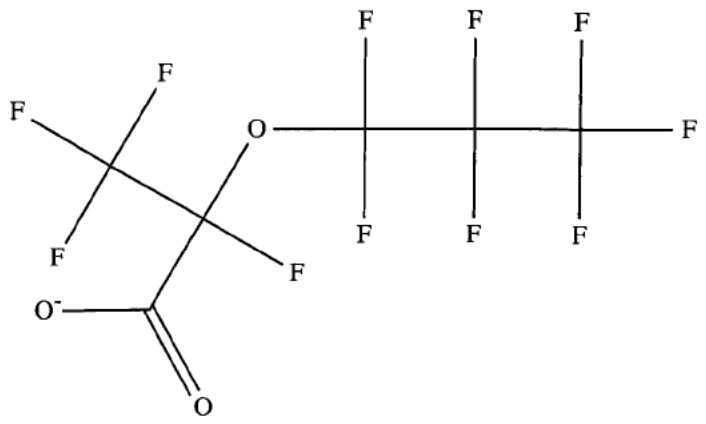
ECOTOX: Predicted (P) and measured (M) toxicity values in mg/L (ppm) are:

fish 96-h LC50	=	60.0	P
fish 96-h LC50	>	96.9	M, O mykiss
daphnid 48-h LC50	=	47.0	P
daphnid 48-h LC50	>	102	M
green algal 96-h EC50	=	12.0	P
green algal 72-h EC50	>	106	M
fish chronic value	=	9.0	P
daphnid ChV	=	7.0	P
algal ChV	=	6.0	P

Predictions are based on SARs for anionic surfactants; SAR chemical class = surfactant - anionic - COO - C8; MW 330; liquid (508)/solid (509) S = 43 mg/L at 25 C (P,508)/dispersible in water (P,509); pH7; effective concentrations based on 100% active ingredients and mean measured concentrations; hardness <180.0 mg/L as CaCO3; and TOC <2.0 mg/L;
moderate concern for toxicity;
assessment factor = 10.0
concern concentration = 1.0 mg/L (ppm)
*CEB ECOTOX: All releases to surface water with CC = 1000 ppb

[redacted]

P08-509

ID	STRUCTURE
[redacted]	
TOX STUDY H	
CAS 062037-80-3	
MOL WEIGHT 347.09	
MOL FORMULA C6 H4 F11 N O3	
8(e)	

ACUTE ORAL STUDY IN RATS - DEATHS WITHIN 3 HOURS AT 7500 MG/KG AND GREATER; ENLARGED LIVERS, CHANGES IN PANCREAS AT DOSES OF 2250 TO 5000 MG/KG

NAME

TETRAFLUORO-2-(HEPTAFLUOROPROPOXY)PROPIONIC ACID, AMMONIUM SALT

GTOX Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 601
P-08-0508	0013252-13-6	06/30/08	Incomplet	

S/A: S

Name of Analog:

Reviewer: KEM

		with activation	without activation	Positive Strains
Salmonella Assay:		☐	☐	
Chromosomal Aberration	CHO:	☐	☐	
	CHL:	☐	☐	
	V79:	☐	☐	
E. coli Reverse Mutation:		☐	☐	
Mouse Micronucleus Assay:	Route: oral		☐	
Rat Hepatocytes Unscheduled DNA Synthesis:			☐	

Other GTOX Results

-A negative in vivo unscheduled DNA synthesis test was conducted in rats with CAS # 62037-80-3.
-A positive in vitro chromosome aberrations assay was provided in human lymphocytes in the presence and absence of activation with [redacted]
-A negative in vivo miconucleus study was provided in a combined 2-week inhalation and micronucleus study in rats with [redacted].

Comments

-Further GTOX information is located in the last record for P-08-508 to 509
-Two chromosome aberrations assays were conducted in CHO cells in which crude industrial grade [redacted] t was positive in the presence and absence of activation, and CAS # 62037-80-3 was positive only in the presence of activation.
-Dose dependant reductions in mitotic indices were observed in an oral mouse micronucleus test, but results were considered negative.

ECOTOX: X

Fate: Ready Biodegradability-CO2 Evolution (p.1022-1053); Hydrolysis (p.1247-1292).

WS/Log P: WS: infinitely soluble (>750-751g/L) @20 +/-0.5C (M, p.1168,1212), LogP: 2 @pH 5, 7.4 (E, p.1079-80); Transformation Byproduct WS: 7.07mg/L @20C (M, p.1663), LogP: 3.83 (M, p.1718)

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 669
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	669

Study Type	Species	Sex	Route
EIRR	RABB	M	EYES

Test Substance Description

[redacted]

Test Conditions

Study duration: 28 hours; Strain: New Zealand White; Wt/Life stage: 2846 g/young adult; No. Groups/No. Per Group: 1/1; Controls: untreated eye; Dose Level: 0.1 mL; Test Conditions (Dose regimen): OECD 405 (acute eye irritation/corrosion). The test substance was placed into the conjunctival sac of the treated eye and observed for the study period. The treated eye was not rinsed after application. Scoring of ocular lesions was done according to the Draize scale.

Results

Brown and white discoloration of the conjunctival membrane of the treated rabbit eye, which appeared to look like necrosis, was observed at 1, 24, and 28 hours after instillation of the test substance. Corneal opacity (score of 2), iritis (score of 1), conjunctival chemosis (score of 2 or 4), and discharge (score of 2 or 3) were also observed. Fluorescein stain examinations of the treated eye were positive for corneal injury. The rabbits were euthanized the day after treatment for humane reasons. The test substance was a positive irritant based on ocular effects and the appearance of necrosis.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 670
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	670

Study Type	Species	Sex	Route
DIRR	RABB	M	DERM

Test Substance Description

[redacted]

Test Conditions

Study duration: 76 hours; Strain: New Zealand White; Wt/Life stage: 3033-3167 g/young adult; No. Groups/No. Per Group: 1/1, 1/2; Controls: NS; Dose Level: 0.5 mL; Test Conditions (Dose regimen): OECD 404 (acute dermal irritation/corrosion). The test substance was applied to the clipped, intact skin of one rabbit for 4 hours with a semi-occlusive bandage. Following this exposure period, the dressing was removed and the site was rinsed and assessed. Upon observation of no severe effects, 2 additional animals were dosed in the same manner. Observations were made 1, 24, 48/50, and 72 hours after patch removal.

Results

Erythema (score of 1 or 2) but no edema was observed in the 3 rabbits on the day of dosing. No dermal irritation was reported during observations. No clinical signs were observed, and no body weight loss occurred. The test substance produced limited irritation based on erythema that cleared within 24 hours.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 671
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	671

Study Type	Species	Sex	Route
ATOX	MICE	F	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 14 days; Strain: Crl:CD1(ICR); Wt/Life stage: 25.1-27.4 g prefast/NS; No. Groups/No. Per Group: 7/1; Controls: NS; Test Conditions (Dose regimen): OECD 425 (Up-and-Down Procedure). The test substance was administered to 1 fasted female mouse at a dose of 175 mg/kg, to 3 fasted female mice at a dose of 550 mg/kg, and to 3 fasted female mice at a dose of 1750 mg/kg. The mice were dosed one at a time at a minimum of 48-hour intervals. The mice were observed for mortality, body weight effects, and clinical signs for up to 14 days after dosing. All mice were necropsied to detect grossly observable evidence of organ or tissue damage.

Results

Death occurred in all 3 mice dosed at 1750 mg/kg. No clinical signs were observed in the mouse dosed at 175 mg/kg or in 2 mice dosed at 550 mg/kg. Wet fur was observed on the day of dosing in 1 mouse dosed at 550 mg/kg. Effects observed prior to death in mice exposed to 1750 mg/kg ranged from no clinical signs to lethargy and low posture. No body weight losses occurred in surviving mice after dosing. No test substance related lesions were found in the study. The estimated LD50 was 1030 mg/kg for female mice.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 672
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 13252-13-6	KEM	672

Study Type	Species	Sex	Route
ATOX	RATS	F	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 17 days; Strain: Crl:CD(SD); Wt/Life stage: 193-226 g/~ 10-11 weeks; No. Groups/No. Per Group: 9/1; Controls: NS; Test Conditions (Dose regimen): OECD 425 (Up-and-Down Procedure). The test substance was administered to 2 fasted female rats at a dose of 175 mg/kg, to 4 fasted female rats at a dose of 550 mg/kg, and to 3 fasted female rats at a dose of 1750 mg/kg. The rats were dosed one at a time at a minimum of 48-hour intervals. The rats were observed for mortality, body weight effects, and clinical signs for up to 17 days after dosing. All rats were necropsied to detect grossly observable evidence of organ or tissue damage. The liver, kidneys, heart, brain, thyroid, complete gastrointestinal tract, ovaries, lungs, and any abnormal tissues were collected from all rats at necrospy. The heart, liver, kidneys, and gross lesions were processed to slides and evaluated microscopically.

Results

Death occurred in 1 rat dosed at 550 mg/kg on test day 2 and in all 3 rats dosed at 1750 mg/kg on the day of dosing. One rat dosed at 550 mg/kg was sacrificed in extremis on day 17 because of excessive body weight loss (~28%) and clinical signs. Clinical signs of toxicity were observed in most rats and included lung noise, clear oral discharge (foamy at times), absent feces, high posture, stained fur/skin, wet fur, closed eyes, lethargy, moribundity, not eating, and/or ataxia. No body weight loss occurred in surviving rats. Gross observations observed in dead rats consisted of discoloration and erosion/ulcer of the stomach glandular mucosa. No gross lesions were observed in surviving rats. Microscopic findings in the stomach of the dead rats included degeneration/necrosis and erosion/ulcer of the glandular mucosa as well as submucosal edema. Minimal to mild acute tubular nephrosis was also observed in dead rats. Fatal acute gastritis was the cause of death in rats found dead. The LD50 was 550 mg/kg for female rats.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 673
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	673

Study Type	Species	Sex	Route
ATOX	RATS	M	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 14 days; Strain: Crl:CD(SD); Wt/Life stage: 268-331 g/NS; No. Groups/No. Per Group: 10/1; Controls: NS; Test Conditions (Dose regimen): OECD 425 (Up-and-Down Procedure). The test substance was administered to 1 fasted male rat at a dose of 175 mg/kg, to 2 fasted male rats at a dose of 550 mg/kg, to 4 fasted male rats at a dose of 1750 mg/kg, and to 3 fasted male rats at a dose of 5000 mg/kg. The rats were dosed one at a time at a minimum of 48-hour intervals. The rats were observed for mortality, body weight effects, and clinical signs for up to 14 days after dosing. All rats were necropsied to detect grossly observable evidence of organ or tissue damage.

Results

One and three rats were found dead following exposure to 1750 and 5000 mg/kg, respectively. Clinical signs observed in all rats up to the day after dosing included lethargy, wet fur, stained fur/skin, lung noise, decreased muscle tone, and/or low posture. No body weight loss occurred in surviving animals. Gross findings including skin stain, expanded lungs, eye discoloration, and/or stomach discoloration were observed at 1750 (1/4) and 5000 (3/3) mg/kg. The LD50 was 1750 mg/kg for male rats in this study.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 674
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	674

Study Type	Species	Sex	Route
ATOX	RATS	F	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 14 days; Strain: Crl:CD(SD); Wt/Life stage: 202-222 g/10-11 weeks; No. Groups/No. Per Group: 8/1; Controls: NS; Test Conditions (Dose regimen): OECD 425 (Up-and-Down Procedure). The test substance was administered to 1 fasted female rat each at a dose of 175 and 550 mg/kg, to 3 fasted female rats at a dose of 1750 mg/kg, and to 3 fasted female rats at a dose of 5000 mg/kg. The rats were dosed one at a time at a minimum of 48-hour intervals. The rats were observed for mortality, body weight effects, and clinical signs for up to 14 days after dosing. All rats were necropsied to detect grossly observable evidence of organ or tissue damage.

Results

The 3 rats dosed at 5000 mg/kg were found dead on days 0 to 2 after dosing. Clinical signs observed in all rats included hair loss, high posture, stained fur/skin, wet fur, lethargy, clear ocular discharge, prostrate posture, partially closed eyes, and/or salivation. No body weight loss occurred after dosing. Gross findings including lung discoloration, discoloration of the mandibular lymph nodes, and discoloration of the lungs and liver was observed in rats found dead. The oral LD50 was 3129 mg/kg for female rats.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	
P-08-0508	0013252-13-6	6/30/2008	Incomplete	ID: Rec# 6 : 675

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	675

Study Type	Species	Sex	Route
ATOX	RATS	M	GAVG

Test Substance Description

Test Conditions

Study duration: 14 days; Strain: ChR-CD males; Wt/Life stage: NS/young adult; No. Groups/No. Per Group: 11/1; Controls: NS; Dose Level: 1.5, 12, 130, 1,000, 2,250, 3,400, 5,000, 7,500, 11,000, 12,963, and 17,000 mg/kg ; Test Conditions (Dose regimen): The test material was administered as an aqueous solution in single doses to rats. Survivors were killed 14 days later.

Results

Animals exposed to 7,500, 11,000, 12,963, and 17,000 mg/kg died. Toxic signs in animals that died included discomfort, and gasping or tonic convulsions. Slightly enlarged livers with enlarged hepatocytes and pronounced cell membranes was observed in dead animals. Additionally, slight to moderate degenerative changes in the pancreas were noted. Toxic signs in animals exposed to non-lethal doses included discomfort, increased water intake, inactivity, polyuria at higher levels, and/or initial weight loss. The approximate lethal dose was 7,500 mg/kg.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 676
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	676

Study Type	Species	Sex	Route
ATOX	RATS	M	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 15 days; Strain: Crl:CD BR; Wt/Life stage: 238-272 g/~7 weeks; No. Groups/No. Per Group: 6/1; Controls: NS; Dose Level: 670, 2,300, 3,400, 5,000, 7,500, 11,000 mg/kg; Test Conditions (Dose regimen): Rats were exposed to a single dose of the test substance. Following administration, rats were observed for clinical signs of toxicity. Surviving rats were weighed and observed daily until signs of toxicity subsided and then at least 3 times a week. Pathological examination was not performed.

Results

Mortality was noted 1 day following dose administration at doses of 5,000 mg/kg and greater. The rat dosed at 11,000 mg/kg exhibited lethargic behavior, low carriage, and low posture within1 hour of dosing. Rats dosed at 2,300 and 3,400 mg/kg exhibited wet, yellow-stained perineum and ruffled fur as well as weight losses of approximately 17% and 14%, respectively, within 1 day of dosing. The clinical signs observed at 2,300 and 3,400 mg/kg cleared within 2 and 4 days of dosing, respectively. No clinical signs of toxicity were noted at the lowest dose.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 677
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	677

Study Type	Species	Sex	Route
ATOX	RABB	M	DERM

Test Substance Description

[redacted].

Test Conditions

Study duration: 15 days; Strain: New Zealand white; Wt/Life stage: 2113-2187 g/young adult; No. Groups/No. Per Group: 1/2; Controls: NS; Dose Level: 5000 mg/kg; Test Conditions (Dose regimen): The test substance was applied to the shaved, intact skin of 2 rabbits, and the site was occluded for approximately 24 hours. The test substance was removed, and rabbits were observed for up to 14 days (weekends excluded).

Results

No mortality or clinical signs of toxicity were observed in either rabbit. Erythema was observed up to observation day 13, but had resolved by the completion of the study. No edema was observed. Epidermal scaling and sloughing were observed in both rabbits from 6 to 13 days after application. One rabbit exhibited a small area of necrosis on days 2 to 6, and by day 7 the area had sloughed off and alopecia remained. The test substance was considered to be slightly toxic (ALD between 5000 and 10,000 mg/kg) when applied to shaved intact skin.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 678
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	678

Study Type	Species	Sex	Route
ATOX	RATS	MF	DERM

Test Substance Description

[redacted]

Test Conditions

Study duration: 15 days; Strain: Crl:CD(SD); Wt/Life stage: males-296 g/9 weeks, females-236 g/10 weeks; No. Groups/No. Per Group: 1/10 (5 male, 5 female); Controls: NS; Dose Level: 5000 mg/kg bw; Test Conditions (Dose regimen): OECD 402 (acute dermal toxicity). The test substance was applied to clipped, intact skin for 24 hours with a semi-occlusive bandage. Following this exposure period, the dressing was removed and the site was rinsed and assessed for up to 14 days. Irritation was scored according to the Draize scale.

Results

No mortality or clinical signs of systemic toxicity were observed, and no body weight loss was noted. No erythema or edema was observed in males. In females, erythema (score of 2) but no edema on the test site was observed. Hyperkeratosis was observed in 8 rats, and ulceration was observed in the test site of 3 rats during the study. All dermal effects resolved by day 13. The LD50 was considered to be greater than 5000 mg/kg bw.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 679
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 13252-13-6	KEM	679

Study Type	Species	Sex	Route
DIRR	NA	NS	INVR

Test Substance Description

[redacted]

Test Conditions

Skin corrosion potential was evaluated in an in vitro International Corrositex assay. The model is based on the time required for the test substance to pass through a biobarrier membrane and produce a change in a chemical detection system. An aliquot of 500 uL of the test substance was applied to each of 4 membrane discs and evaluated.

Results

The test substance passed through all 4 of the membranes. The mean breakthrough time for all 4 vials was 1 hour, 8 minutes, and 13 seconds. Under the conditions of this test, the test substance is corrosive.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 680
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	680

Study Type	Species	Sex	Route
OTHR	RATS	MF	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 168 hours; Strain: Crl:CD(SD); Wt/Life stage: NS/7-12 weeks; No. Groups/No. Per Group: 2/6 (3 males, 3 females); Controls: NS; Dose Level: 10 (low dose), 30 (high dose) mg/kg; Test Conditions (Dose regimen): A biopersistence and pharmokinetic screen was conducted. Rats were exposed to a single dose of the test substance in water. Blood was sampled at 0, 0.25, 0.5, 1, 2, 4, 8, 12, 24, 48, 72, 96, 120, 144, and 168 hours after exposure. Fat and liver were analyzed for parent compound to provide an estimate of tissue:plasma ratio.

Results

Clearance time was 12 and 4 hours for males and females of the low dose group, respectively. Clearance time was 22 and 8 hours for males and females of the high dose group, respectively. All fat samples were below the level of quantification (LOQ). The tissue/plasma ratio was 2.2 for low dosed males, 0.8 for high dosed males, and could not be calculated for females since female plasma was below the LOQ.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 681
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 13252-13-6	KEM	681

Study Type	Species	Sex	Route
OTHR	RATS	MF	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 168 hours; Strain: Crl:CD(SD); Wt/Life stage: NS/7-12 weeks; No. Groups/No. Per Group: 2/6 (3 males, 3 females); Controls: NS; Dose Level: 10 (low dose), 30 (high dose) mg/kg; Test Conditions (Dose regimen): A biopersistence and pharmokinetic screen was conducted. Rats were exposed to a single dose of the test substance in water. Blood was sampled at 0, 0.25, 0.5, 1, 2, 4, 8, 12, 24, 48, 72, 96, 120, 144, and 168 hours after exposure. Fat and liver were analyzed for parent compound to provide an estimate of tissue:plasma ratio.

Results

Clearance time was 28 and 8 hours for males and females of the low dose group, respectively. Clearance time was 22 and 4 hours for males and females of the high dose group, respectively. All fat samples were below the level of quantification (LOQ). The tissue/plasma ratio was 0.64 for low dosed males, 0.71 for high dosed males, and could not be calculated for females since female liver concentrations were below the LOQ.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 682
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 13252-13-6	KEM	682

Study Type	Species	Sex	Route
STOXRPDS	MICE	M	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 7 days; Strain: Crl:CD1(ICR); Wt/Life stage: NS/ ~ 6 weeks; No. Groups/No. Per Group: 2/5; Controls: vehicle control group; Dose Level: 30 mg/kg-bw/day; Test Conditions (Dose regimen): Animals were repeatedly administered the test substance for 7 days.

Results

No deaths or treatment-related clinical signs were noted. Body weights were significantly increased compared to controls on day 7. Statistically significant and test substance-related organ weight changes were limited to the liver, which had approximately 2-fold elevations in al liver weight parameters. Microscopic changes were limited to the liver and included minimal single cell necrosis of hepatocytes, moderate hepatocellular hypertrophy, and moderate increases in mitotic figures. These changes occurred in mice administered to 30 mg/kg-bw/day dose and were not seen in controls. Minimal vacuolation of hepatocytes was present in 2/5 treated mice; however, it is uncertain as to whether this change is test substance-related.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 683
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	683

Study Type	Species	Sex	Route
STOXRPDS	MICE	M	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 7 days; Strain: Crl:CD1(ICR); Wt/Life stage: NS/ ~ 6 weeks; No. Groups/No. Per Group: 2/5; Controls: vehicle control group; Dose Level: 30 mg/kg-bw/day; Test Conditions (Dose regimen): Animals were repeatedly administered the test substance for 7 days.

Results

No deaths or treatment-related clinical signs were noted. Body weights were significantly increased compared to controls on day 7. Statistically significant and test substance-related organ weight changes were limited to the liver, which had approximately 2-fold elevations in al liver weight parameters. Microscopic changes were limited to the liver and included minimal single cell necrosis of hepatocytes, moderate hepatocellular hypertrophy, and moderate increases in mitotic figures. These changes occurred in mice administered to 30 mg/kg-bw/day dose and were not seen in controls. Minimal vacuolation of hepatocytes was present in 1/5 treated mice; however, it is uncertain as to whether this change is test substance-related.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 684
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 13252-13-6	KEM	684

Study Type	Species	Sex	Route
STOXRPDS	RATS	MF	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 14 days; Strain: Crl:CD(SD); Wt/Life stage: NS /~6 weeks; No. Groups/No. Per Group: 4/10 (5 males, 5 females; main study) and 1/6 (3 males, 3 females; metabolism study); Controls: vehicle control; Dose Level: 0, 30, 100 or 300 mg/kg-bw/day (main study) and 30 mg/kg-bw/day (metabolism study); Test Conditions (Dose regimen): In the main study, the test substance was administered to control, low-, mid-, and high-dose groups from day 0 to day 6. Additional low-dose animals were administered the test substance from day 0 to day 7 in the metabolism study.

Results

No deaths occurred, no adverse test substance-related changes were observed for in-life parameters and no effects on body weights were noted. Statistically significant decreases in some red cell mass parameters were observed in male and female rats at the high-dose level. A statistically significant increase in red cell distribution width was also present in high-dose females. Decreases in serum lipids (triglycerides and/or cholesterol) were present in all dosed male groups. Other changes in clinical chemistry parameters occurred at 30 and/or 300 mg/kg-bw/day and included increased ALKP and BUN and decreased bilirubin, creatinine, total protein, globulin and calcium. Increased liver weight parameters were present in males at all dose levels and in high-dose females. Increased kidney weights were also present in all male dose groups. Microscopic findings were limited to hepatocellular hypertrophy in all treated male and female dose groups. Lesions were graded as mild in all male groups and as minimal in all female groups. The clearance time of the analytes for males and females was 24 and 4 hours, respectively. 96- and 120-hour female plasma concentrations were below LOQ. The LOQ is approximately 20 ng/mL. The total P450 increased in all treated males. B-oxidation was increased in all treated males and in high-dose females as well as low-dose males following 7 days of recovery.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 685
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	685

Study Type	Species	Sex	Route
STOXRPDS	RATS	MF	GAVG

Test Substance Description

[redacted]

Test Conditions

Study duration: 14 days; Strain: Crl:CD(SD); Wt/Life stage: NS / ~6 weeks; No. Groups/No. Per Group: 4/10 (5 males, 5 females; main study) and 1/6 (3 males, 3 females; metabolism study); Controls: vehicle control; Dose Level: 0, 30, 300 or 1000 mg/kg-bw/day (main study) and 30 mg/kg-bw/day (metabolism animals); Test Conditions (Dose regimen): In the main study, the test substance was administered to control, low-, mid-, and high-dose groups from day 0 to day 6. Additional low-dose animals were administered the test substance from day 0 to day 7 in the metabolism study.

Results

No deaths occurred. High-dose male rats exhibited a significant decrease in body weight gain. No treatment-related clinical observations were observed in either sex at any dose level. Statistically significant decreased in red cell mass parameters (red blood cell, hemoglobin and hematocrit) were observed in male rats at 300 and 1000 mg/kg-bw/day and in females at 1000 mg/kg-bw/day. Red cell distribution width, reticulocytes and neutrophils were also increased high-dose females. All treated males and females at 300 and 1000 mg/kg-bw/day showed a decrease in serum lipids (triglycerides and/or cholesterol) and globulins. Other changes in clinical chemistry parameters occurred at the two highest dose levels and include increased ALT, AST, BUN and glucose and decreased SDH, creatinine and calcium. Increased liver parameters were present in males at all dose levels and in high-dose females. Other organ weight changed included decreases in heart weight parameters in high-dose males and increase in some kidney weigh parameters in high-dose females. Histopathological changes were limited to minimal to mild hepatocellular hypertrophy in the liver of male rats at all doses and in high-dose females and were associated with increases in B-oxidation and/or increases in total P450 enzyme activity. The clearance time of the analytes for males and females was 46 and 4 hours, respectively. The 46-hour clearance time was impacted by one male having a slightly higher AUC than the other 2 individuals. It is likely that the calculated clearance time of 46 hours is longer than the true value due to the low number of animals in the study (n = 3). The plasma concentration on 2 consecutive days of dosing was similar, implying that there is no accumulation in the rat following repeated dosing. The LOQ is approximately 20 ng/mL. Total P450 was increased in both sexes at the highest dose and in males at the mid-dose. B-oxidation was increased in all treated males and in high-dose females.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 686
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 62037-80-3	KEM	686

Study Type	Species	Sex	Route
DSEN	MICE	F	DERM

Test Substance Description

[redacted]

Test Conditions

Study duration: 5 days; Strain: CBA/JHsd; Wt/Life stage: 19.9-23.8 g/ 9 weeks; No. Groups/No. Per Group: 6/5; Controls: vehicle control and positive control (25% hexylcinnamaldehyde in DMF); Dose Level: 0, 5, 25, 50 or 100%; Test Conditions (Dose regimen): OECD 429 local lymph node assay in mice- The test substance was administered to both ears of the animals for 3 consecutive days. On test day 5, mice received 3H-Thymidine by tail vein injection and were sacrifice approximately 5 hours later, at which time the cell proliferation in the draining auricular lymph nodes was evaluated.

Results

No death or clinical signs of toxicity was observed. A statistically significant increase in mean body weight gains compared to the vehicle control group was observed at 25% test concentration. Although statistically significant increases in cell proliferation measurements compared to the vehicle control group were observed at the 50% and 100% test concentrations, stimulation indices (SIs) of less than 3.0 were observed at all concentrations. Therefore, the EC3 value was not calculable. A 25% concentration of the positive control, HCA, produced a dermal sensitization response in mice. Under the conditions of this study, the test substance did not produce a dermal sensitization response in mice. Thus, the test substance is not considered to be a dermal sensitizer in mice.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 687
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S	CAS # 13252-13-6	KEM	687

Study Type	Species	Sex	Route
DSEN	MICE	F	DERM

Test Substance Description

[redacted]% p[redacted]

Test Conditions

Study duration: 5 days; Strain: CBA/JHsd; Wt/Life stage: 18.3-23.5 g/8 weeks; No. Groups/No. Per Group: 7/5; Controls: negative vehicle control, positive control (25% hexylcinnamaldehyde in AOO) and positive vehicle control (AOO); Dose Level: 0, 10, 25, 50 or 100%; Test Conditions (Dose regimen): OECD 429 local lymph node assay in mice- The test substance was administered to both ears of the animals for 3 consecutive days. On test day 5, mice received 3H-Thymidine by tail vein injection and were sacrifice approximately 5 hours later, at which time the cell proliferation in the draining auricular lymph nodes was evaluated.

Results

Statistically significant decreases in mean body weight gains compared to the vehicle control group were observed in the 100% and positive vehicle control groups. Following the second application, one mouse from the 100% group exhibited signs of lethargy, ruffled fur, dehydration and wet fur (ventral). This animal was later found dead. Bright red lungs were observed during gross pathology. Following the third application, 2 mice from the 50% group were found dead. Gross pathology findings were bright, red lungs and no abnormality detected, respectively. During the course of the study, 2 mice from the 50% group and 2 mice from the 100% group exhibited signs of wet fur and perineum. Additionally, one animal also exhibited bilateral hair loss of the forelimb. Statistically significant increases in cell proliferation measurements compared to the vehicle control group were observed at 25%, 50% and 100%. Stimulation indexes of greater than 3.0 were observed at 50% and 100%. The EC3 value was calculated to be 37%. A 25% concentration of the positive control, HCA, produced a dermal sensitization response. Under the conditions of this study, the test substance produced a dermal sensitization response in mice and therefore is considered to be a dermal sensitizer.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 688
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
A	[redacted]	KEM	688

Study Type	Species	Sex	Route
STOXRPDS	RATS	M	INHL

Test Substance Description

[redacted]

Test Conditions

Study duration: 28 days; Strain: Crl:CDBR; Wt/Life Stage: 192-231g/ 7 weeks; No Groups/No. per group: 4/10 and 1/5; Controls: air control and untreated control group; Dose Level: 0, 5000, 25,000 or 175,000 ppm; Test conditions (dose regimen): Test substance vapor was administered to animals for 6 hours/day, 5 days/week for 2 weeks. Five rats per group were sacrificed following the exposure period and the remaining 5 rats were sacrificed following a 14-day recovery period. Immediately following the 10th inhalation exposure, one femur form each of five rats per group was removed during necropsy and bone marrow smears were prepared for micronucleus evaluation. An additional group of 5 male rats served as a positive indicator group for micronucleus induction.

Results

No adverse effect in clinical chemistry, hematology, urine analytical measurements, urinary fluoride or body weights were observed. High-dose animals showed a lack of response to an altering stimulus and occasional tremors during exposure. No effects were observed in the rat micronucleus evaluation. The NOAEL was considered to be 25,000 ppm.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 689
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
A	[redacted]	KEM	689

Study Type	Species	Sex	Route
STOXRPDS	RATS	M	INHL

Test Substance Description

[redacted]

Test Conditions

Study duration: 28 days; Strain: Crl:CDBR; Wt/Life Stage: 192-231g/ 7 weeks; No Groups/No. per group: 2/10 and 1/5; Controls: air control and untreated control group; Dose Level: 0 or 25000 ppm; Test conditions (dose regimen): Test substance vapor was administered to animals for 6 hours/day, 5 days/week for 2 weeks. Five rats per group were sacrificed following the exposure period and the remaining 5 rats were sacrificed following a 14-day recovery period. Immediately following the 10th inhalation exposure, one femur form each of five rats per group was removed during necropsy and bone marrow smears were prepared for micronucleus evaluation. An additional group of 5 male rats served as a positive indicator group for micronucleus induction.

Results

No adverse effect in clinical chemistry, hematology, urine analytical measurements, urinary fluoride or body weights were observed. Immediately after the 2-week exposure period, rats exposed to 28 showed a small increase (approximately 9%) in liver weights compared to controls. The liver weight increase was no longer observed in this group after a 2-week recovery period. In the absence of corresponding cytopathology or liver enzyme changes, the increased liver weights were considered to be of questionable toxicological significance and may have been an adaptive metabolic response to the high-dose and, therefore, not considered an adverse effect. No effects were observed in the rat micronucleus evaluation. The NOAEL was considered to be 25,000 ppm.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 1
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		KEM	1

Study Type	Species	Sex	Route
OTHR	RATS	MF	INVR

Test Substance Description

[redacted]

Test Conditions

Study duration: 2 hours; Strain: Crl:CD(SD)IGS BR rats; Wt/Life stage: N/A; No. Groups/No. Per Group: 3 test, 1 biotransformation; Controls: 3 heat-inactivated controls, 1 positive control (4-nonylphenol); Dose Level: 2 uM (694 ppb) for clearance incubation, 200 uM (69.4 ppm) for biotransformation incubations; Test Conditions (Dose regimen): An in vitro rat hepatocyte screen was conducted in order to estimate metabolic clearance of the test compound in rat hepatocytes and extrapolate results to whole animal and to identify metabolites and describe probable metabolic pathways for the compound tested. A cell concentration of 1x10^6 cells/mL for clearance incubation and 5x10^6 cells/mL for biotransformation incubations was reported. Incubation temperature was 37C.

Results

No apparent loss of the parent compound was observed within 2 hours of incubation compared to heat-inactivated controls. No metabolites were identified in the biotransformation incubation samples.

Toxicology Report

PMN No.	CAS No.	Rcvd:	OECD	ID: Rec# 6 : 722
P-08-0508	0013252-13-6	6/30/2008	Incomplete	

S/A	Name of Analog	Reviewer	Study#:
S		KEM	722

Study Type	Species	Sex	Route
OTHR	OTHR	NS	OTHR

Test Substance Description

Test Conditions

Other GTOX Results (cont.):
-Salmonella assays were negative with and without activation for CAS# 13252-13-6 (P-08-0508), CAS # 62037-80-3 (P-08-0509), and [redacted].
-E.coli mutagenicity tests were negative for CAS# 13252-13-6 (P-08-0508) and CAS # 62037-80-3 (P-08-0509).
-In vitro mammalian chromosome aberration tests in Chinese Hamster Ovary cells were conducted, which were positive(?) for polyploidy with and without activation for CAS# 62037-80-3 (P-08-0509) and Crude Industrial Grade HFPODA Ammonium Salt (H-27529), positive for structural aberrations with activation and negative without activation for CAS# 62037-80-3, and negative for structural aberrations with and without activation for H-27529.
-A negative in vivo oral chromosome aberrations assay was conducted in mice with CAS# 62037-80-3

Results

NCSAB SAT REPORT		CBI? (Y/N):
PMN:	P-08-0508	CAS RN: 13252-13-6

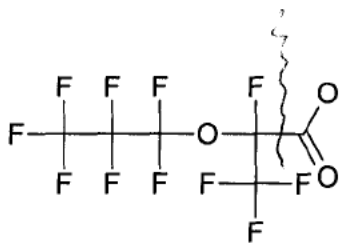
Chemical Name:

Propanoic acid, 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy)-

Analogs:

Production Volume: [redacted]

Structure:



CLOGP = 5.03 ≈ C8

Use:

[redacted]

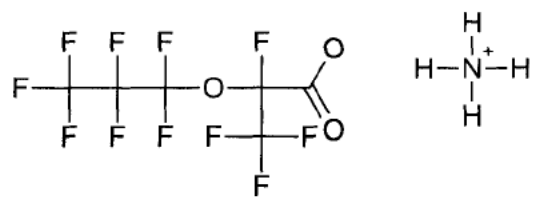
Formula:	$C_6HF_{11}O_3$	Eq Wt:	
Mol Weight:	330.06	Wt%<500:	Wt%<1000
MP:		BP: [redacted]	VP: [redacted]
H2O Sol (g/L):	0.043	Physical State: Liquid	Log P: 8.12 (ACD)

Endpoint (mg/L)	Est. Value	Meas. Value	Comments
Fish 96-h	60		
Daphnid 48-h	47		
Algal 96-h	12		
Fish ChV	9.0		
Daphnid ChV	7.0		
Algal ChV	6.0		
BCF			

CHEMICAL CLASS:				SAR: surf - anionic - COO
ECOTOX CONCERN	H	(M)	L	CONCERN CONCENTRATION 0.60
DATE 7/11/08				ASSESSOR:

NCSAB SAT REPORT		CBI? (Y/N):
PMN: P-08-0509	CAS RN:	62037-80-3
Chemical Name: Propanoic acid, 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy)-, ammonium salt (1:1)	Analogs:	
	Production Volume: [redacted]	

Structure:



CLOGP = 5.03 ≈ C8

Use:

Polymerization aid - [redacted]

Formula: $C_6H_4F_{11}NO_3$	Eq Wt:		
Mol Weight: 347.09	Wt%<500:		Wt%<1000
MP:	BP:		VP: 0.000042
H2O Sol (g/L): Dispersible	Physical State: Solid		Log P:

Endpoint (mg/L)	Est. Value	Meas. Value	Comments
Fish 96-h	60		
Daphnid 48-h	47		
Algal 96-h	12		
Fish ChV	9.0		
Daphnid ChV	7.0		
Algal ChV	6.0		
BCF			

CHEMICAL CLASS:				SAR: surf-anionic-COO
ECOTOX CONCERN	H	(M)	L	CONCERN CONCENTRATION 0.60
DATE 7/11/08				ASSESSOR:

P08-0508
EVALUATION OF ECOTOXICITY STUDIES
Friday, July 11, 2008
Evaluator: S. Cragg

Test Type	Function Evaluated	Parameter Measured	Limit Test Measured Value (mg/L)	ECOSAR Predicted Value (mg/L)
Acute Freshwater Copepod (*Daphnia magna*)	Mobility	48-hr EC50 NOEC	> 102 102	46
Acute Freshwater Fish (*Oncorhynchus mykiss*)	Lethality	96-hr LC50 NOEC	> 96.9 96.9	60
Acute Freshwater Algae (*Pseudokirchneriella subcapitata*)	Growth Inhibition Growth Rate†	72-hr ErC50	>106	12
	Growth Rate	NOEC	106	
	Biomass†† (as area under curve)	0-72-hr EbC50	>106	
		NOEC	106	

* No effects at saturation.

† Concentration that reduced specific growth rate by 50%.

†† Concentration that reduced biomass by 50%.

Conclusion: Results from the three limit tests are considered valid. There were no effects at the highest concentrations tested for all three species, which was approximately 100 mg/L. A concentration of concern (CoC) may be derived from these studies. Since the actual 50% effect concentrations could not be determined (because they were somewhere above the limit test concentrations; i.e., the NOEC), the NOEC may be used instead to derive the CoC. The NOEC of 100 mg/L is divided by a factor of 10 to simulate a chronic value. The resulting simulated chronic value is divided again by a assessment factor of 10 to derive the concentration of concern, which is 1.0 mg/L (ppm) or 1,000 ug/L (ppb).

OPPT STRUCTURE ACTIVITY TEAM (SAT) MEETING DATE 7-11-08

	ATTENDEES	SIGNATURE
	CHEMISTRY	
___	Paul Bickart	
___	Diana Darling	
___	Rich Engler	
___	Greg Fritz	
___	Daniel Lin	
✓	Kathy Schechter	Kathy Schechter
___	_____	
	ENVIRONMENTAL FATE	
___	Bob Boethling	
___	Wen-Hsiung Lee	
___	Laurence Libelo	
✓	David Lynch	David G. Lynch
___	Andy Mamantov	
✓	Jed Costanza	Jed Costanza
	HEALTH	
___	Katherine Anitole	
✓	Michael Cimino	
✓	Steve Cragg	Steve Cragg
___	Leonard Keifer	
___	David Lai	
✓	Jim Murphy	
___	Deborah Norris	
✓	Ronald Ward	
___	Yin Tak Woo	
___	_____	
___	_____	
	ENVIRONMENTAL EFFECTS	
X	Gordon Cash	MEMO
___	Maggie Wilson	
___	_____	
___	_____	
	SAT CHAIR/OTHER	
___	Rebecca Jones	
✓	Leonard Keifer	
___	Jim Kwiat	
___	_____	
✓	Tracey Pennington	Tracy Pennington

P08-508

ID [redacted]	STRUCTURE [redacted]
CAS [redacted]	
MOL WEIGHT [redacted]	
POINTER PMN	
MOL FORMULA [redacted]	
SAT HEALTH 2-3	
SAT ECO 2	
DISPO	KWD
[redacted]	LIVER LUNG DEVEL UNCERT-SENS-CARDIAC/NEURO AQUATOX-A,C
COMMENTS	
NAME	
[redacted]	

GTOX Report

PMN No. [redacted] CAS No. [redacted] Rcvd: 01/01/95 OECD COMPLET ID: Rec# 8 : 154

S/A: N Name of Analog: Reviewer: XXX

		with activation	without activation	Positive Strains
Salmonella Assay:		☐	☐	
Chromosomal Aberration	CHO:	☐	☐	
	CHL:	☐	☐	
	V79:	☐	☐	
E. coli Reverse Mutation:		☐	☐	
Mouse Micronucleus Assay:	Route:		☐	
Rat Hepatocytes Unscheduled DNA Synthesis:			☐	

Other GTOX Results

Comments

ECOTOX: [X]

Fate: Fate data included in submission

WS/Log P:

Toxicology Report

[redacted]

Rcvd: 01/01/95

OECD COMPLETE

ID: Rec# 8 : 154

S/A: A

Name of Analog: [redacted]

Reviewer: xxx

Study#: 633

Study Type	Species	Sex	Route
Acute Toxicity	Rat	M	Oral (unspec)

Test Substance Description

Test Conditions

0

Results

Deaths occurred in males at dosages of 60 mg/kg or greater.

Toxicology Report

[redacted]

Rcvd: 01/01/95

OECD COMPLETE

ID: Rec# 8 : 154

S/A: A

Name of Analog: [redacted]

Reviewer: XXX

Study#: 634

Study Type	Species	Sex	Route
ADME	Rabbit	NS	Dermal

Test Substance Description

Test Conditions

Skin absorption

Results

ALD = 130 mg/kg.

Toxicology Report

[redacted]

Rcvd: 01/01/95

OECD COMPLETE

ID: Rec# 8 : 154

S/A: A

Name of Analog: [redacted]

Reviewer: xxx

Study#: 635

Study Type	Species	Sex	Route
Subchronic Toxicity	Rat	NS	Inhalation

Test Substance Description

Test Conditions

Dose: 5, 50, 500 ppb; Doses were given 6 h/day, 5 days/week for 2 weeks

Results

Histopathologic evaluations of the liver revealed changes ?
characterized by swollen, eosinophilic hepatocytes which had a ?
granular cytoplasm.

ID [redacted]	STRUCTURE [redacted]
CAS [redacted]	
MOL WEI [redacted]	
POINTER PMN	
MOL FORMULA [redacted]	
SAT HEALTH 3	
SAT ECO 3	
DISPO	KWD
[redacted]	BLOOD LIVER KIDNEY MUTA ONCO IMMUNO DEVEL REPRO LUNG AQUATOX-A,C
COMMENTS	
NAME	

[redacted]

GTOX Report

PMN No. [redacted] CAS No. [redacted] Rcvd: 11/14/07 OECD Incomplet ID: Rec# 6 : 552

S/A: S Name of Analog: Reviewer: JVR

		with activation	without activation	Positive Strains
Salmonella Assay:		N	N	
Chromosomal Aberration	CHO:			
	CHL:	P	P	
	V79:			
E. coli Reverse Mutation:		N	N	
Mouse Micronucleus Assay:	Route:			
Rat Hepatocytes Unscheduled DNA Synthesis:				

Other GTOX Results

Comments: Biodeg OECD301C

ECOTOX:

Fate:

WS/Log P: WS: Soluble in water (MSDS; pg. 23)

Toxicology Report

PMN No. [redacted] CAS No. [redacted] Rcvd: 11/14/07 OECD Incomplete ID: Rec# 6 : 552

S/A: S Name of Analog: Reviewer: JVR Study#: 558

Study Type	Species	Sex	Route
Repeated Dose Toxicity	Rat	MF	Gavage

Test Substance Description: [redacted]

Test Conditions

Study duration: 6 weeks; Strain: Crl:CD(SD); Wt/Life Stage: 132.7- 365.6 g/5 weeks ; No Groups/No. per group: 6/10 ; Controls: purified water (vehicle and recovery control); Dose range: 0 (vehicle), 5, 25 or 100 mg/kg/day; Test conditions (dose regimen): The test substance was administered daily to rats by oral gavage for 28 days followed by a 14-day recovery period. Observations were made on clinical signs, sensorimotor functions, body weight, food intake, hematology, blood chemistry, urinalysis and pathology. Doses were based on results from a previously conducted 14-day repeated oral dose toxicity study in rats at 50, 250, 500 or 1000 mg/kg/day.

Results

Hematological findings in the 100 mg/kg group included decreased RBC and Ht in males and females, increased Reticulo in females and prolonged PT in males. Changes in blood chemistry included increased ALT and A/G ratio and decreased T-Cho in males of the 100 mg/kg group. Absolute and relative kidney weights were increased in males treated with 25 mg/kg or more and absolute and relative liver weights were increased in males in the 100 mg/kg. At necropsy, observations of the high dose group included an elevation in and hyperplasia of (squamous epithelium) the limiting ridge in the forestomach in males and females and enlargement of the liver in males. Diffuse hypertrophy of hepatocytes with granular degeneration in males and focal necrosis of hepatocytes in females were observed in the 100 mg/kg group. In the recovery test, all observed changes were completely reversible. NOEL = 5 mg/kg/day.

Toxicology Report

PMN No. [redacted]

Rcvd: 11/14/07

OECD: Incomplete

ID: Rec# 6 : 552

S

Reviewer: JVR

Study#: 559

Study Type	Species	Sex	Route
Other	Rat	MF	Other

Test Substance Description

[redacted]

Test Conditions

Study duration: 5 days; Strain: CrlCD(SD); Wt/Life Stage: 157-248 g/ 7 weeks ; No Groups/No. per group: 1/18 and 1/6 ; Controls: N/S; Dose Level: 10 mg/kg; Test conditions (dose regimen): Pharmacokinetic study; The test substance (0.5 mL) was administered intravenously once to a pharmacokinetic (blood collection) group and an excretion group. Following treatment, observations were made up to 48 hours at which time animals were euthanized. Parameters evaluated included clinical observations, body weights, food consumption, toxicokinetics, pharmacokinetic profile (blood chemistry) and excretion profile (urinalysis).

Results

Systemic exposure was 7 times higher in males than in females, the test substance remaining mostly in the circulation of male rats but having extensive tissue distribution in female rats. The terminal elimination phase in serum had a half-life of 9.4 and 5.4 hours for female and male rats, respectively. The half-life in urine was 1.8 and 5.4 hours for females and males, respectively. Overall, elimination in the urine of both sexes was 65% and most of the test substance was eliminated over 12 hours post-dosing in both sexes. The elimination of the test substance in the urine appeared to be mono-exponential for male rats and was not log-linear for females.

Toxicology Report

[redacted] Rcvd: 11/14/07 OECD Incomplete ID: Rec# 6 : 552

S/A: S | Name of Analog: | Reviewer: JVR | Study#: 560

Study Type	Species	Sex	Route
Other	Monkey	MF	Other

Test Substance Description

[redacted]

Test Conditions

Study duration: 20 days; Strain: cynomolgus; Wt/Life Stage: 2003- 2751g/2.5-3.5 years; No Groups/No. per group: 1/6; Controls: N/S; Dose Level: 10 mg/kg; Test conditions (dose regimen): Pharmacokinetic study; Following a 13-day acclimation/pretest period (at which time physical examinations were performed), the test substance (5 mL/kg) was administered intravenously once to one group of monkeys. Observations were made up to 7 days post-dosing. Parameters evaluated included clinical observations, body weights, toxicokinetics, excretion profile (urinalysis) and pharmacokinetic profile (blood chemistry).

Results

All animals survived. Pharmacokinetic parameters in serum were similar between genders; male monkeys appeared to have a higher exposure and longer half-life than female monkeys. On average, about 60-65% of the administered dose was recovered in the urine during the 7 days post-dosing.

Toxicology Report

[redacted]

Rcvd: 11/14/07

OECD: Incomplete

ID: Rec# 6 : 552

Reviewer: JVR

Study#: 561

S

Study Type	Species	Sex	Route
Acute Toxicity	Rat	MF	Gavage

Test Substance Description

[redacted]

Test Conditions

Study duration: 12 hours; Strain: Sprague-Dawley CD (Crl:CD(SD) IGS BR); Wt/Life Stage: 203-294 g/ 8-12 weeks; No Groups/No. per group: 1/3 and 2/3; Controls: N/S; Dose Level: 300 or 2000 mg/kg; Test conditions (dose regimen): OECD TG 423 "Acute Oral Toxicity"; The test substance (10 mL/kg) was administered to the first group of three animals at the high dose level by oral gavage. Based on the effects, a second group was administered a lower dose in the same manner. Upon observation of no severe effects, another group was dosed in the same manner at the same low dose level. Observations were made up to 4 hours post-dosing, at which time they were euthanized.

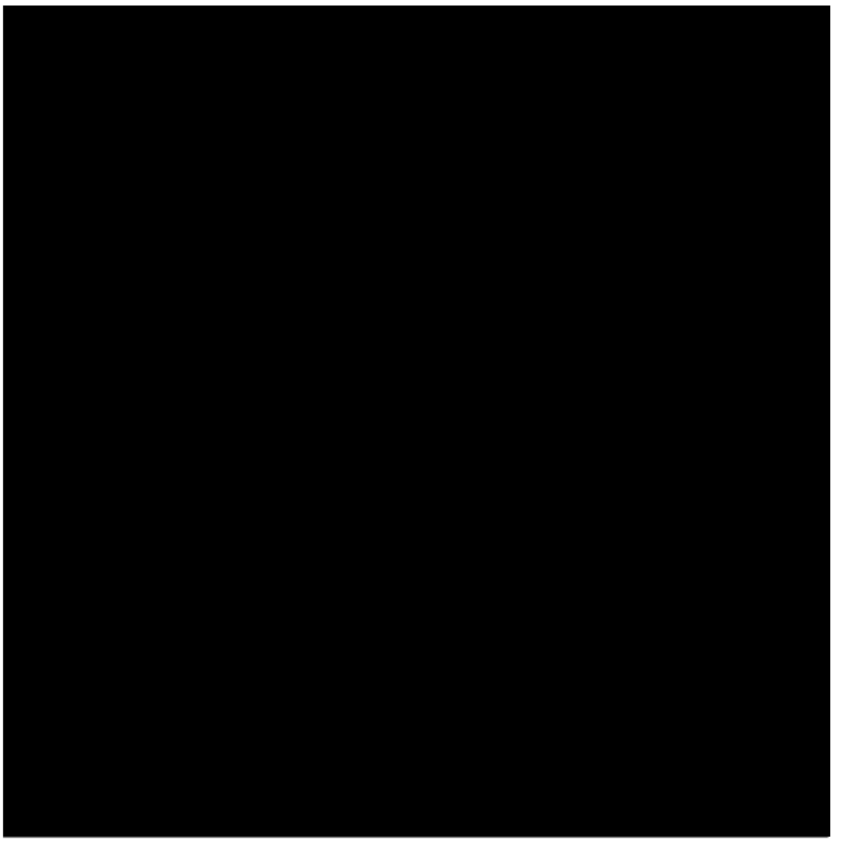
Results

All animals treated at 2000 mg/kg died one of which was killed in extremis. No deaths were noted in animals treated at the 300 mg/kg dose level. Two high dose animals exhibited hunched posture, ataxia, lethargy, decreased respiratory rate, noisy respiration, dehydration and diuresis. Abnormalities noted at necropsy of the animals that died during the study were abnormally red lungs, dark liver, dark kidneys and clear liquid present in the stomach. LD50 = 500 mg/kg

ID [redacted]	STRUCTURE [redacted]
TOX STUDY [redacted] H	
CAS	
MOL WEIGHT [redacted]	
MOL FORMULA [redacted]	
8(e)	

INHALATION APPROXIMATE LETHAL CONCENTRATION = 400 PPM, LIVER ENLARGEMENT AT 100 PPM SEVERE SKIN IRRITANT

NAME [redacted]

ID	STRUCTURE
TOX STUDY [redacted] H	
CAS [redacted]	
MOL WEI [redacted]	
MOL FORMULA [redacted]	
8(e)	

7-DAY ORAL STUDY IN RATS (30, 100, 300 MG/KG), THE STUDY INCLUDED A PHARMACOKINETIC EVALUATION AT 30 MG/KG - HEPATOCELLULAR HYPERTROPHY, INCREASED LIVER beta-OXIDATION AND TOTAL P450 ACTIVITIES, INCREASED KIDNEY AND LIVER WEIGHTS IN ALL DOSE GROUPS; CLINICAL CHEMISTRY AND CHANGES IN RED BLOOD CELL PARAMETERS WERE ALSO REPORTED

NAME

[redacted]

ID	STRUCTURE
[redacted]	
TOX STUDY	
H	
CAS	
MOL WEIGHT [redacted]	
MOL FORMULA [redacted]	
8(e)	

28-DAY ORAL STUDY IN RATS (5, 20, 80 MG/KG) - SEVERE TOXICITY WITH SACRIFICE OF ANIMALS ON DAY 23 AT 80 MG/KG; LIVER TOXICITY IN ALL DOSE GROUPS; HEMATOLOGIC EFFECTS AT 20 AND 80 MG/KG CORROSIVE TO THE SKIN ORAL LD50 IS BETWEEN 200 AND 2000 MG/KG POSITIVE IN AN IN VITRO CHROMOSOME ABERRATION STUDY IN V79 CHINESE HAMSTER CELLS NEGATIVE IN THE AMES TEST

NAME

[redacted]

ID [redacted]	STRUCTURE [redacted]
TOX STUDY [redacted] H	
CAS	
MOL WEIGHT [redacted]	
MOL FORMULA [redacted]	
8(e)	

5-DAY ORAL STUDY IN RATS (29, 91, 288 MG/KG) - ALL MALES AND 2 OF 6 FEMALES DIED AT 288 MG/KG WITH GI AND ADRENAL EFFECTS; NO DEATHS AT 29 OR 91 MG/KG

NAME

[redacted]

ID	STRUCTURE
[redacted]	[redacted]
TOX STUDY H	
CAS	
MOL WEIGHT [redacted]	
MOL FORMULA [redacted]	
8(e)	

28-DAY ORAL STUDY IN RATS (5, 50, 150, 750 MG/KG) - ALL ANIMALS SACRIFICED IN EXTREMIS IN WEEK 2 AT 750 MG/KG; REDUCTION IN PROSTATE AND SEMINAL VESICLE SIZE, REDUCED EPIDIDYMIDES WEIGHTS, ADRENAL AND OVARY WEIGHTS, THYMUS AND SPLEEN WEIGHTS AT 150 MG/KG; ON-GOING STUDY

NAME

[redacted]

OPPT STRUCTURE ACTIVITY TEAM (SAT) MEETING DATE 7-11-08

	ATTENDEES	SIGNATURE
CHEMISTRY		
___	Paul Bickart	
___	Diana Darling	
___	Rich Engler	
___	Greg Fritz	
___	Daniel Lin	
✓	Kathy Schechter	Kathy Schechter
___		
ENVIRONMENTAL FATE		
___	Bob Boethling	
___	Wen-Hsiung Lee	
___	Laurence Libelo	
✓	David Lynch	David G. Lynch
___	Andy Mamantov	
✓	Jed Costanza	Jed Costanza
HEALTH		
___	Katherine Anitole	
✓	Michael Cimino	Michael Cimino
✓	Steve Cragg	Steve Cragg
___	Leonard Keifer	
___	David Lai	
✓	Jim Murphy	Jim Murphy
___	Deborah Norris	
✓	Ronald Ward	Ronald Ward
___	Yin Tak Woo	
___		
___		
ENVIRONMENTAL EFFECTS		
X	Gordon Cash	MEMO
___	Maggie Wilson	
___		
___		
SAT CHAIR/OTHER		
___	Rebecca Jones	
✓	Leonard Keifer	Leonard Keifer
___	Jim Kwiat	
✓	Tracey Pennington	Tracey Pennington